

What is claimed is:

1. A method of detecting abnormal cell growth in a mammal, comprising
5 assessing the level of Pin1 in a test sample from the mammal, wherein an elevation in the levels of Pin1 is indicative of abnormal cell growth.

2. The method of claim 1, wherein the level of Pin1 is a protein level.

10 3. The method of claim 1, wherein the level of Pin1 is a nucleic acid level.

4. The method of claim 1, wherein the test sample is an epithelial cell test sample.

15 5. The method of claim 1, wherein the test sample is a body fluid test sample selected from the group consisting of a blood, ascites, or brain body fluid test sample.

6. The method of claim 1, wherein the abnormal cell growth is benign.

20 7. The method of claim 1, wherein the abnormal cell growth is a malignant cancer.

8. The method of claim 7, wherein the cancer selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track or testicular cancer.

25 9. The method of claim 7, wherein the cancer is colon cancer.

10. A method of detecting abnormal cell growth in a mammal, comprising the steps of:

30 (a) detecting a level of Pin1 in a test sample; and
(b) comparing the level of Pin1 in the test sample with a control level, and wherein a difference in the level of Pin1 in the test sample is indicative of abnormal cell growth in the mammal.

35 11. The method of claim 10, wherein the level of Pin1 is a protein level.

12. The method of claim 10, wherein the level of Pin1 is a nucleic acid level.

13. The method claim 10, wherein the abnormal cell growth is a malignant cancer.

14. The method claim 13, wherein the cancer is selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer.

15. The method of claim 13, wherein the cancer is colon cancer.

16. A method of detecting abnormal cell growth in a mammal by assessing the level of Pin1 protein in a test sample from the mammal, comprising the steps of:

(a) contacting the test sample with an antibody having specificity for Pin1 under conditions suitable for binding of the antibody to Pin1 thereby resulting in the formation of a complex between the antibody and Pin1;

(b) detecting the complex between the antibody and Pin1; and

(c) comparing the amount of the complex in the test sample with an amount of a complex in a control sample,

wherein an elevation in the amount of the complex between the antibody and Pin1 in the test sample compared to the complex in the control sample is indicative of abnormal cell growth.

17. The method of claim 16, wherein the antibody is a polyclonal antibody.

18. The method of claim 16, wherein the antibody is a monoclonal antibody.

19. The method of claim 16, wherein the abnormal cell growth is a malignant cancer.

20. The method of claim 19, wherein the cancer is selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer.

21. The method of claim 19, wherein the cancer is colon cancer.

22. The method of claim 16, wherein the antibody is detectably labeled.

23. The method of claim 22, wherein the detectable label is selected from the group consisting of a radioactive, enzymatic, biotinylated and fluorescent label.

24. The method of claim 23, wherein the complex is detected by incubating the complex with a second antibody specific for the complex, wherein the secondary antibody comprises a detectable label.

25. A method of detecting abnormal cell growth in a mammal, comprising the steps of:

a) detecting a level of Pin1 nucleic acid in a test sample; and
b) comparing the level of Pin1 in the test sample with a level of Pin1 in a control sample,
wherein an elevation in the level of Pin1 in the test sample compared to the control sample is indicative of abnormal cell growth.

26. The method of claim 25, wherein the method further comprises performing a polymerase chain reaction with oligonucleotide primers capable of amplifying the Pin1 nucleic acid prior to detection.

27. A method of determining abnormal cell growth in a mammal, comprising the steps of:

a) contacting a test sample obtained from the mammal with a nucleic acid probe to a Pin1 nucleic acid;
b) maintaining the test sample and the nucleic acid probe under conditions suitable for a hybridization;
c) detecting the hybridization between the test sample and the nucleic acid probe; and
d) comparing the hybridization in the test sample from the mammal to a control test sample without the cellular proliferation,
wherein an elevation in the hybridization signal in the test sample from the mammal compared to the control sample is indicative of abnormal cell growth.

28. A method of determining a stage of an abnormal cell growth, comprising assessing a level of Pin1 in a test sample from a mammal.

29. The method of claim 28, wherein the stage of the abnormal cell growth is a stage of abnormal breast or prostate cancer cell growth.

30. The method of claim 28, wherein the level of Pin1 is a protein level.

31. A method of determining a stage of abnormal cell growth in a mammal by assessing the level of Pin1 in a test sample from the mammal, comprising the steps of:

contacting the test sample with an antibody having specificity for Pin1 under conditions suitable for binding of the antibody to Pin1 thereby resulting in the formation of a complex between the antibody and Pin1; and

comparing the amount of the complex in the test sample with an amount of a complex in a control sample,

wherein an elevation in the amount of the complex in the test sample compared to the control sample is indicative of the stage of abnormal cell growth.

32. The method of claim 31, wherein the antibody is a monoclonal antibody.

33. The method of claim 31, wherein the complex is detected by incubating the complex with a second antibody specific for the complex wherein the secondary antibody comprises a detectable label.

34. The method of claim 31, further comprising determining a ratio of the amount of Pin1 bound to a Pin1 antibody to an amount of a non-Pin1 cellular protein selected from the group consisting of actin or tubulin.

35. A method of determining a stage of abnormal cell growth in a mammal, comprising assessing a level of a Pin1 nucleic acid in a test sample, comprising the steps of:

performing a polymerase chain reaction with oligonucleotide primers capable of amplifying the Pin1 nucleic acid;

detecting a level of amplified nucleic acid fragments of the Pin1 nucleic acid; and comparing the level of amplified nucleic acid fragments in the test sample to a sample comprising varying stages of the abnormal cell growth,

wherein the stage of abnormal cell growth in the mammal is determined.

36. A method of determining a stage of abnormal cell growth in a mammal, comprising the steps of:

contacting a test sample obtained from the mammal with a nucleic acid probe to a Pin1 nucleic acid;

maintaining the test sample and the nucleic acid probe under conditions suitable for hybridization of the probe to Pin1 nucleic in the sample;

detecting the hybridization between the Pin1 nucleic acid of the test sample and the nucleic acid probe; and

comparing the hybridization in the test sample from the mammal to hybridization of the nucleic probe to Pin1 in a control, wherein the control sample comprises varying stages of the abnormal cell growth, thereby determining the stage of the abnormal cell growth in the mammal.

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37. A method of evaluating the efficacy of a treatment of abnormal cell growth in a mammal, comprising comparing a level of Pin1 in at least two test samples, wherein the test samples comprise a first test sample obtained at a first time and a second test sample obtained at a later second time, wherein a decrease in the level of Pin1 between the two test samples indicates the efficacy of the treatment of the abnormal cell growth in the mammal.

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38. The method of claim 37, wherein the level of Pin1 is a protein level.

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39. A kit for determining a stage of abnormal cell growth in a mammal comprising one or more reagents for detecting a level of Pin1 in a test sample obtained from the mammal.

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40. A kit for evaluating the efficacy of a cancer treatment in a mammal, comprising one or more reagents for detecting a level of Pin1 in a test sample obtained from the mammal.

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41. A kit for distinguishing between an abnormal cell growth and a normal cell growth in a mammal comprising one or more reagents for detecting a level of Pin1 in a test sample obtained from the mammal.

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42. The kit for determining the extent of metastasis of abnormal cell growth in a mammal, comprising one or more reagents for detecting a level of Pin1 in a test sample obtained from mammal.

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43. A method for facilitating the diagnosis of a state associated with abnormal cell growth in a subject, comprising detecting the level of a Pin1 marker in a sample from the subject as an indication of whether the subject has a state associated with abnormal cell growth, thereby facilitating the diagnosis of the subject.

44. The method of claim 43, wherein the subject is receiving, or has received, therapy for a state associated with abnormal cell growth and the diagnosis is used to evaluate the subject's response to the therapy.

45. The method of claim 43, wherein the subject is involved in a therapy agent clinical trial and the diagnosis is used to evaluate the effectiveness of an agent of the clinical trial.

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46. A method for facilitating the diagnosis of cancer in a subject, comprising detecting the level of a Pin1 marker in a sample from the subject as an indication of whether the subject has cancer, thereby facilitating the diagnosis of the subject.

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47. The method of claim 46, wherein the subject is receiving, or has received, therapy for cancer and the diagnosis is used to evaluate the subject's response to the therapy.

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48. The method of claim 46, wherein the subject is involved in a clinical trial of a cancer therapy agent and the diagnosis is used to evaluate the effectiveness of an agent of the clinical trial.

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49. The method of claim 46, wherein the Pin1 marker is a marker capable of facilitating the diagnosis of a plurality of cancers.

50. The method of claim 46, wherein the Pin1 marker is a marker capable of facilitating the diagnosis of more than one type of cancer.

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51. The method of claim 46, wherein the Pin1 marker is a marker capable of facilitating the diagnosis of more than two types of cancer.

52. The method of claim 46, wherein the Pin1 marker is a marker capable of facilitating the diagnosis of more than three types of cancer.

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53. The method of claim 46, wherein the Pin1 marker is a marker capable of facilitating the diagnosis of more than four types of cancer.

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54. The method of claim 46, wherein the level of Pin1 marker detected is used to stage the cancer.

55. The method of claim 46, wherein the diagnosis involves a prediction of whether the cancer is or will become metastatic.

56. A method of treating a subject for a state associated with abnormal cell growth, comprising administering a Pin1 modulator to the subject such that the state associated with abnormal cell growth is treated.

5 57. The method of claim 56, wherein the Pin1 modulator is a Pin1 inhibitor.

58. A method of treating a subject for cancer, comprising administering a Pin1 modulator to the subject such that the cancer is treated.

10 59. The method of claim 58, wherein the Pin1 modulator is a Pin1 inhibitor.

60. The method of claim 58, wherein the cancer is selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer.

15 61. The method of claim 58, wherein the cancer is colon cancer.

62. A packaged kit for carrying out a method of claim 43 or 46, wherein the kit comprises

- 20 a) at least one reagent for assaying levels of Pin1 in a sample from a subject, and
b) instructions for using the at least one reagent to assay levels of Pin1 in a sample from a subject for the described method.

25 63. The packaged kit of claim 62 wherein the at least one reagent is a polyclonal antibody.

64. The packaged kit of claim 62 wherein the at least one reagent is a monoclonal antibody.

30 65. A packaged kit for carrying out a method of claims 56 or 58, wherein the kit comprises

- a) at least one Pin1 modulator, and
b) instructions for using the Pin1 modulator in the described method.

35 66. The method of claim 56 or 58, wherein the method is carried out in combination with at least one additional agent.

67. The method of claim 66, wherein the additional therapeutic agent is an ACI agent.

68. The method of claim 67, wherein the additional ACI agent is not a Pin1 modulator.

69. (Amended) A method of detecting abnormal cell growth in a mammal, comprising assessing the level of Pin1 in a test sample from the mammal, wherein an elevation in the levels of Pin1 in said mammal when compared to a control sample is indicative of abnormal cell growth.

70. The method of claim 69, wherein the test sample is an epithelial cell test sample.

71. The method of claim 69, wherein the test sample is a body fluid test sample selected from the group consisting of a blood, ascites, or brain body fluid test sample.

72. The method of claim 69, wherein the abnormal cell growth is benign.

73. The method of claim 69, wherein the abnormal cell growth is a malignant cancer.

74. The method of claim 73, wherein the cancer selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track or testicular cancer.

75. The method of claim 73, wherein the cancer is colon cancer.

76. A method of detecting abnormal cell growth in a mammal, comprising the steps of:

- (a) detecting a level of Pin1 in a test sample; and
- (b) comparing the level of Pin1 in the test sample with a control sample

and wherein a difference in the level of Pin1 in the test sample when compared to a control sample is indicative of abnormal cell growth in the mammal.

77. The method claim 75, wherein the abnormal cell growth is a malignant cancer.

78. The method claim 76, wherein the cancer is selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer.

79. The method of claim 76, wherein the cancer is colon cancer.

80. A method of detecting abnormal cell growth in a mammal by assessing the level of Pin1 protein in a test sample from the mammal, comprising the steps of:

(a) contacting the test sample with an antibody having specificity for Pin1 under conditions suitable for binding of the antibody to Pin1 thereby resulting in the formation of a complex between the antibody and Pin1;

(b) detecting the complex between the antibody and Pin1; and

(c) comparing the amount of the complex in the test sample with an amount of a complex in a control sample,

wherein an elevation in the amount of the complex between the antibody and Pin1 in the test sample compared to the complex in the control sample is indicative of abnormal cell growth.

81. The method of claim 79, wherein the antibody is a polyclonal antibody.

82. The method of claim 79, wherein the antibody is a monoclonal antibody.

83. The method of claim 79, wherein the abnormal cell growth is a malignant cancer.

84. The method of claim 82, wherein the cancer is selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer.

85. The method of claim 82, wherein the cancer is colon cancer.

86. The method of claim 79, wherein the antibody is detectably labeled.

87. The method of claim 85, wherein the detectable label is selected from the group consisting of a radioactive, enzymatic, biotinylated and fluorescent label.

88. The method of claim 86, wherein the complex is detected by incubating the complex with a second antibody specific for the complex, wherein the secondary antibody comprises a detectable label.